

JAPANESE PATENT OFFICE

PATENT ABSTRACTS OF JAPAN

(11) Publication number:

57021320 A

(43) Date of publication of application: 04.02.1982

(51) Int. CI

A61K 31/13

A61K 31/165

(21) Application number:

55093853

(71) Applicant: CHUGAI PHARMACEUT CO LTD

(22) Date of 2001

11.07.1980

(72) Inventor: **HONDA NARIMITSU**

NAGAI HIDEAKI

HINOHARA YOSHIKAZU

KOIZUMI MASUO MURAKAMI YASUSHI

NAKANO HIDEKI

(54) BLOOD SUGAR LEVEL DEPRESSING AGENT

COPYRIGHT: (C)1982,JPO&Japio

(57) Abstract:

PURPOSE: To provide a blood sugar level depressing agent containing a VSHR; Fbenzamide derivative as an active component.

CONSTITUTION: An agent containing the compound of formula [R₁ and R₂ are H, alkyl, (substituted) aralkyl, or (substituted) phenyl] as an active component. The compound of formula has excellent insulin biosynthesis promoting activity and blood sugar level depressing activity. It is effective at a dose of 0.IW100mg/kg for man, and maintains the activity for ≥24hr by the administration of 0.1W100mg/kg, once a day. The compound of formula can be prepared easily e.g. by reducing the corresponding m-nitrobenzoic acid amide by conventional method.

⑩ 日本国特許庁 (JP)

10特許出願公開

⑩ 公開特許 公報 (A)

昭57-21320

⑤Int. Cl.³ A 61 K 31/13

識別記号 ADP ADP 庁内整理番号 6408-4 C 6408-4 C ③公開 昭和57年(1982)2月4日発明の数 1審査請求 未請求

(全 4 頁)

多血糖降下剤

20特

 ℓ , \cdot

願 昭55—93853

②出 願昭55(1980)7月11日

31/165

⑫発 明 者 本多成光

東京都豊島区高田3丁目41番8 号中外製薬株式会社綜合研究所 内

@発 明 者 永井秀明

東京都豊島区高田3丁目41番8 号中外製薬株式会社綜合研究所 内

⑫発 明 者 日野原好和

東京都豊島区高田3丁目41番8

号中外製薬株式会社綜合研究所 内

⑫発 明 者 小泉益男

東京都豊島区高田3丁目41番8 号中外製薬株式会社綜合研究所 内

⑩発 明 者 村上泰

東京都豊島区高田3丁目41番8 号中外製薬株式会社綜合研究所 内

⑪出 願 人 中外製薬株式会社

東京都北区浮間5丁目5番1号

⑪代 理 人 安藤憲章

最終頁に続く

明細 #

1. 発明の名称

血糖降下剤

2. 特許請求の範囲

一般式

(式中、R1及びR2は同一又は異って、水栗原子、 直鎖・分枝鎖・環状アルキル落、核に置換基を有 し得るアラルキル蒸又は置換蒸を有し得るフェニ ル基を示す。)で表わされる化合物を有効成分と する血糖降下剤。

3. 発明の詳細な説明

本発明は、次の一般式

$$\sum_{R_0}^{NH_2} -coN \binom{R_1}{R_2} \qquad [1]$$

(式中、R1及びR2は同一又は異って、水業原子, 直鎖・分岐鎖・環状アルキル基,核に置換差を有 し得るアラルキル基又は置換基を有し得るフェニル基を示す。) で要わされる化合物を有効成分とする血糖降下剤の発明である。

上式(1)で表わされる化合物の中には、公知の 化合物が含まれるが、それらの記載されている先 行文献には血糖降下作用ないしそれを示唆する果 理作用は全く記載されていない。

上式 (1) で 表わされる本発明の 化合物は、 例えば、 以下の 参考 例 に 示すように、 対応するメタニト ロ 安 息 香酸 アミド 類を 常法により 還元する ととにより 容易に 得る ととができる。

5 ml 及びアセトン 2 0 0 ml の混合格液に、氷冷機 拌下、メタニトロペンゾイルクロライド 1 8.6 9 を徐々に加える。同温度で 3 0 分、次いで室温で 1 時間境拌後反応格液を 1 g の水に注ぎ、析出す

イソプロピルアミン68 , トリエチルアミン1

る結晶を伊取し、水疣後再結晶して無色針状晶の メタニトロ - N - イソブロビルベンズアミド(融

点131~132℃)1879を得た。との5.2

8、10%パラジウム-炭素 0.5 P 及びエタノール 100 efの a 液に水素を通じ、常法により接触 選元する。計算量の水素を吸収後触媒を除去し、反応液を放圧機縮し、残産をエタノールより再結晶して無色針状晶のメタアミノ・N・イソブロビルベンズアミド(化合物 1) 4.1 P を得た。 融点 148~149℃.

元素分析値 分子式 C10 H14 N2 O として

с н м

理輪億份 67.38 7.92 15.72

突側値(%) 67.35 7.94 15.69

上配と同様にして表1の化合物を得た。

なお、化合物 2 5 , 2 7 及び 2 9 は油状で得られたので表中にハイマススペクトルの値を、欄外に N M R の値を記載した。



 β^n i

化合物	假换基	及び競換位置	t 分子式	融 点 (37)	収率 (%)	元素分析值					
ML	R ₁	R ₂				理 0	論 値 H	(94) N	· 実 0	侧值 H	(%) N
2	н	н	C7 H 8 N 2 O	77~78	8 1	6175	5.9 2	2 0.5 8	6 1.7 1	5.96	2 0.5 5
3	,	СН3	O 8 H 10 N 2 O	121~122	8 5	6398	6.71	18.65	6392	6.68	18.69
4	.,	C ₂ H ₅	C ₉ H ₁₂ N ₂ O	70~71	7 6	6 5.8 3	7.3 7	17.06	6 5.7 2	7.2 8	1 7.1 9
5	•	#-C3 H7	C10 H14N2 O	57~58	7 8	6 7.3 8	7.92	1 5. 7 2	6 7.2 5	7.8 8	1 5.6 4
6	,	n-C4 H9	C11H16N2O	112~118	7 5	6 8.7 2	8.39	1 4.5 7	68.70	8.3 7	1 4.5 0
7	,	sec -04 Hg	•	109~111	7 4		•		68.67	8.44	1465
8	•	t -O4 H9	•	126~127	7 9		,		68.69	8.36	1 4.5 1
9	,	6-04H9	•	87~89	7 6		•		68.75	8.46	1 4.6 2
10		€	C13H18N2O	147~148	8 4	7 1.5 2	8.3 1	1283	7 1.5 8	8.35	1 2 7 6
11	•	⊘	C 13 H 12 N2 O	132~133	8 6	7356	5.7 0	13.20	7350	5.67	13.26
1 2	,	Can,	O14H14 N2O	88~89	8 4	7 4.3 1	6.24	1238	74.24	6.20	13.45

	慢换基	及び資換位置		(4)	収塞		元	苯 :	分析(*	
Ma	R ₁	R ₂	分子式.	ື (ອ)ື້	(%)	理 C	验(使) H	%) N	0 実	例(被 H	(94) N
1 3	Н	OCH,	O 15 H 16 N 2 O 3	83~84	7 6	6 6. 1 6	5.9 2	1 0.2 9	6 5.9 8	5.8 8	1 0.3 5
1 4	•	CONH	O14 H13 N2 O2	180~182	5 6	6 5.8 7	5.13	1 6.4 6	6 5.7 5	5.1 8	1 6.5 5
1 5	•	CONH	•	135~136	5 9		•		6 5. 7 9	5.1 0	1 6.5 2
16		-CONH2		223~226	6 8				6 5.8 1	5.0 7	1 6.5 3
1 7	•	NH.	C18 H18 N3 O	151~153	7 9	68.70	5.77	1 8.4 9	6 8. 6 4	5.79	18.43
18	•	-Ø ^{NH} 2	,	130~131	7 1		,		6 8.7 7	5.70	1853
1 9	•	-NH ₂	,	150~151	7 4		,		6 8.7 5	5.67	1 8.4 2
2 0	,	C00H	O 14 H 12 N 2 O 3	231~233	5 9	6 5, 6 2	4.7 2	1 0.9 3	6 5.7 1	4.6 6	1 1.0 2
2 1	•	- CH ₂	O14 H14 N2O	96~97	7 3	7 4. 3 1	6.24	1238	7 4. 2 5	6.19	1249
2 2	•	-снз-СН3	C ₁₅ H ₁₆ N ₂ O	94~95	8 0	7 4.9 7	6.71	1 1.6 6	74.92	6.75	1161
2 3	•	-CH2	C ₁₅ H ₁₆ N ₂ O ₂	109~110	7 9	7 0.2 9	6.29	10.93	7 0.3 4	6.3 2	1 0. 8 9
2 4	,	-on-Co	0 14 H 13 Of N2 O	131~132	6 7	64.49	5.03	1 0.7 5	6 4.4 2	5.00	1 0.7 9

	體機業及	機機等及び債換位置				元 幸 分 祈 镇					
Ala	R ₁	R ₂	分子式	(10)	収率 (%)	理論(MECNA) OHN	寒 胡 (134) C H N				
2 5	н	- CH2 CH2-	C ₁₅ H ₁₆ N ₂ O	oil	6 2	ハイマススペクトル 2 4 0.1 2 5 9	(*1) 2 4 0.1 2 4 6				
2 6	он 3	СНэ	OgH 12 N2 O	87~88	8 2	6 5.8 3 7.3 7 1 7.0 6	65.78 7.41 17.12				
2 7	n-03H7	n-C3H7	⁶ C ₁₃ H ₂₀ N ₂ O	oil	7 6	ハイマススペクトル 2 2 0.1 5 7 1	(*2) 2 2 0 1 5 8 0				
2 8	6-03H7	6-C3H7	•	179~180	8 0	70.87 9.15 12.72	70.79 9.15 12.78				
2 9	s-O4 H9	a-O4H9	C ₁₅ H ₂₄ N ₂ O	oil	7 4	ハイマススペクトル 248.1883	(#3) 2 4 8 1 8 7 5				
3 0	4-C4H9	1-C4H9	•	85~86	7 9	7254 9.74 11.28	72.48 9.79 11.34				

*1: NMR(CDC\$3)8:7.55~6.40(10H, aromatic-H, -CONH-), 3.75(2H, s, -NH2), 3.45(2H, t, J=6Hs, -CH2-), 2.75(2H, t, J=6Hs, -CH2-)

* 2: NMR (CDC4₃) 8: 7.35~6.50(4H, aromatic -H), 3.90(2H, s.-NH₂), 3.30(4H, t, J=6Hz, (-CH₂OH₃OH₃)×2), 1.60(4H, sextet, J=6Hz, (-OH₂OH₂OH₃)×2), 0.85(6H, t, J=6Hz, (-OH₂OH₂OH₂OH₂)×2)

表 2

投与化合物	血糖值(mg/dl) mean ± S. E. M.	庇しようインスリン (#U/at) mean ± S. B. M.
正常マウス	157± 6	199±40
なし(対照)	3 8 6 ± 2 1	4 3 ± 2 5
1	2 2 4 ± 1 9 ***	1 7 6 ± 3 7°
2	157±16***	1 5 3 ± 4 6
3	260±33*	2 1 3 ± 4 8*
4	2 4 8 ± 4 7 *	1 9 2 ± 5 4
1 0	263±36*	2 0 1 ± 3 8°
1 2	265±32*	2 5 3 ± 5 6*
1 8	166±35***	1 9 0 ± 5 1*
2 1	150 ± 6 ***	2 2 4 ± 3 0 **
2 4	1 9 3 ± 4 1 **	173±63
2 5	2 1 0 ± 3 9 **	184±48*
2 6	2 6 7 ± 5 3	2 2 0 ± 3 7**

*: P < 0.05 **: P < 0.01 ***: P < 0.001

とのようにして得られる本発明の化合物は、優れたインスリン生合成促進作用及び血糖降下作用を有し、ヒトに対しては 0.1~100 m/ b で有めて、1日1回 0.1~100 m / b の投与で24時間以上その効力を持続する。

投与に際しては、通常の製剤化に用いられる慣用手段により所望の剤形に成形された製剤が用い られる。

実施例 1.

1群5匹の5超令DDY系マウス(雄,体重25~30分)を16時間絶食後、本発明化合物(200両ノタ)の水溶液又はけん凋液を経口投与し、20分後にストレプトゾトシン200両ノタを静脈内に投与した。24時間後に心臓から採血し、グルコースオキシダーゼ法により血中補量を、また、二抗体法により血しようインスリン量を倒定した。測定結果を要2に例示する。

なお、表中の化合物番号は参考例の化合物番号 に対応している。

実 照 例 2

メタアミノベンズアミド(化合物2)1 0 0部リン酸水染カルシウム5 8.5 部結晶セルロース5 0 部コーンスターチ4 0 部ステアリン酸カルシウム1.5 部

これらをよく混合し、常法により1錠250mmに打錠(有効成分100mm含有)し、血糖降下用錠剤として用いる。

実施例 3.

メタアミノ - N - ペンジルペンズアミド(化合物 2 1)の 4 0 % 水溶液を調製し、1 アンブルに 2 ml ずつ封入し、減 歯して血糖降下用注射剤として用いる。

出顧人 中外製薬株式会社

代理人 安藤 意章

第1頁の続き

⑩発 明 者 中野英樹

東京都豊島区高田3丁目41番8 号中外製薬株式会社綜合研究所 内

DRAFT TRANSLATION from

RISING SUN COMMUNICATIONS LTD.

(Incorporating Rotha Fullford Leopold of Canberra, Australia)

40 Bowling Green Lane, London EC1R 0NE

JAPANESE PATENT APPLICATION

No. J57-021320

A HYPOGLYCEMIC AGENT

(21) Filing no.: 55-93853

(22) Filing date: July 11, 1980.

(43) Specification published: February 4, 1982.

(72) Inventor(s):

Narumitsu HONDA

c/o Chugai Pharmaceutical General Laboratories.

3-41-8, Takada, Toshima-ku, Tokyo.

Hideaki NAGAI

c/o Chugai Pharmaceutical General Laboratories.

3-41-8, Takada, Toshima-ku, Tokyo.

Masuo KOIZUMI

c/o Chugai Pharmaceutical General Laboratories.

3-41-8, Takada, Toshima-ku, Tokyo.

Yasushi MURAKAMI

c/o Chugai Pharmaceutical General Laboratories.

3-41-8, Takada, Toshima-ku, Tokyo.

Hideki NAKANO

c/o Chugai Pharmaceutical General Laboratories.

3-41-8, Takada, Toshima-ku, Tokyo.

(71) Assignee(s):

Chugai Pharmaceutical KK.

5-5-1 Ukima, Kita-ku, Tokyo.

Examination request: not yet made

Number of Invention: 1

(Total 4 pages)

(51) Int.Cl.³ Identification JPO
Code classification
A61K 31/13 ADP 6408-4C
31/165 6408-4C

Please Note- Names of Japanese firms, research laboratories and government entities, as translated are not necessarily identical with the names adopted by such organisations for international contacts. Japanese personal and surnames often permit of several readings and the ones used in this translation are not necessarily the ones preferred by their bearers. Foreign names mentioned in Japanese specifications cannot always be accurately reconstructed.

. 4. . .

2

Specification

1. Title of Invention

A hypoglycemic agent.

2. Patent Claims

A hypoglycemic agent containing as effective component a compound represented by general formula

$$\sum_{con}^{NH_2} con \begin{pmatrix} R_1 \\ R_2 \end{pmatrix}$$
 [1]

(wherein, R₁ and R₂ may be the same or different and denote a hydrogen atom, a straightchain, branched-chain or cyclic alkyl group, an aralkyl group which can have a substituent in the nucleus, or a phenyl group which may be substituted).

3. Detailed explanation of the invention

This invention is a hypoglycemic agent containing as effective component a compound represented by general formula

$$\bigotimes_{R_2}^{NH_2} con \binom{R_1}{R_2} \qquad [1]$$

(wherein, R_1 and R_2 may be the same or different and denote a hydrogen atom, a straightchain, branched-chain or cyclic alkyl group, an aralkyl group which can have a substituent in the nucleus, or a phenyl group which may be substituted).

Among the compounds represented by aforesaid formula [I], a well known compounds are included, however, hypoglycemic action or a pharmacological action that suggests this are not described whatsoever in the prior publications describing those compounds.

The compounds represented by aforesaid formula [I] can be easily obtained for example by reduction by conventional method of corresponding meta-nitrobenzoic acid amide species as shown in the Reference Example below.

Reference Example

Into a mixed solution of 6 g isopropylamine, 15 ml triethylamine and 200 ml acetone was gradually added 18.6 g meta-nitrobenzoyl chloride under ice cooling and stirring, the mixture was stirred at the same temperature for 30 minutes and then at room temperature for one hour, thereafter, the reaction liquor was discharged into 1 litre of water, precipitated crystals were recovered by

filtration, washed with water, thereafter recrystallised, and meta-nitro-N-isoproylbenzamide (m.p. 131-132°C) 18.7 g was thereby obtained as colourless acicular crystals. Hydrogen was passed though a mixed liquor of 5.2 g of said amide, 0.5 g of 10 % palladium-carbon and 100 ml ethanol, and catalytic reduction was carried out by conventional method. After theoretical quantity hydrogen was absorbed, catalyst was eliminated, the reaction liquor was concentrated under reduced pressure, the residue was recrystallised from ethanol, and thereby meta-amino-N-isoproyl benzamide (compound 1) 4.1 g was obtained as colourless acicular crystals. m.p. 148-149°C.

3

Elemental analysis: as molecular formula C₁₀H₁₄N₂O

	С	Н	N
Calculated values (%)	67.38	7.92	15.72
Measured values (%)	67.35	7.94	15.69

Compounds of Table 1 were obtained in the same way as above.

wherein, compounds 25, 27 and 29 were obtained as oily substances, the value of high mass spectra are shown in the Table and the NMR values are shown below the Table.

Table 1

					ÇD-con (MH³	A1 A2	[1])				
	omp.		stituent	Molecular	m.p.	Yield				nalysis v		
N	0.	_	osition	formula	(°C)	(%)	C	Calc. (H	%) N	Meas C	ured (' H	%) N
ľ	2	R ₁	R ₂	G, H, N, O	77~78	8 1	6 L 7 5	5.92	2058	6 1 7 1	B.9 6	20.55
1	3		OH ₂	Os Has Na O	121~122	8 5	6398	6.71	18.65	6392	6.68	1869
-	4	•	OgHa	O, H12 N2 O	70~71	7 6	6 5.8 3	7.3 7	17.06	6 5.7 2	7,2 8	17.19
	5		n-СэЙ7	O10 H14N2 O	57~58	7.8	6 7.3 8	7.9 2	1 5.7 2	67.25	7.8 8	15.64
	6	,	a-C4H9	C11 H16 N2 O	112~113	7 5	68.72	B.39	1 4.5 7	68.70	8.37	1450
Ì	7	•	sac -04 Hs	•	109~111	7 4		,		6867	8.44	1465
	8	,	1-O4H9	•	126~127	7 9		•		68.69	8.3 6	1 4.5 1
	9	, .	4-04He	,	87~89	7 6		,		68.75	8.4 6	1 4.6 2
	10	,	-⊕	C12H12N2O	147~148	8 4	7 1.5 2	8.3 1	12.83	7 1.5 8	8.35	1276
	11	,	- O	C 12 H 12 N2O	132~133	8 6	7356	5.70	13.20	7350	5.67	1326
	1 2	,	-Qu	014H14N2O	88~8 B	84	74.31	6.24	1238	7424	6.20	13.45
	omp.		stituent	Molecular	m.p.	Yield (%)				nalysis		0/\
N	o.	and t	oosition	formula	(°C)	(%)		Calc. (%)	Meas		%)
						(70)			N		•	•
		R ₁	R ₂			(/ v)	C	Н	N	C	H H	N
	1 3		R ₂	0 18 H 16 N 2 O 3	83~84	-	С	H		С	H Ì	N
	13	R ₁	R2		83~84		C	H	N	C	н	N N
		R ₁	R ₂	O 16 H 16 N2 O2		7 6	C 0 66.16	Н н 6.92	10.29	C 0 65.98	Н н 5.8 8	N N 10.35
	14	R ₁	R2 SCH COMP CONNA CONNA	O 16 H 16 N2 O3	180~182	76	C 0 66.16	H 6.92 5.13	10.29	65.98	Н н 5.8 8 5.1 8	1 6.5 5
	14	н	R2 SCH COMP COMP COMP COMP COMP Mrs COMP Mrs	O 16 H 16 N 2 O 3	180~182	7 6 5 6 5 9	C 0 66.16	H 6.92 5.13	10.29	65.98 65.75	5.88 5.18	N 10.36 16.55
	1 4 1 5 1 6	R ₁	R2 SCH COMP CONNA CONNA	O 15 H 16 N 2 O 3 O 14 H 13 N 3 O 2	180~182 135~136 223~226	7 6 5 6 5 9 6 8	66.16 65.87	H 6.92 5.13	10.29 16.46	C c c c c c c c c c c c c c c c c c c c	H H 5.88 5.18 5.10 5.07	N N 10.35 16.55 16.52 16.53
	1 4 1 5 1 6	R ₁	R2 SCUS COMMS	O 16 H 16 N 2 O 3 O 14 H 19 N 9 O 2	180~182 135~136 223~226 151~153	7 6 5 6 5 9 6 8 7 9	66.16 65.87	H H 6.92	10.29 16.46	C 0 65.98 65.75 65.79 65.81	H 5.88 5.18 5.10 5.07 5.79	N N 10.35 16.55 16.52 16.53
	14 15 16 17	R ₁	R2 6CHs COMB COMB COMB COMB COMB COMB COMB COMB	O 15 H 16 N 2 O 3 O 14 H 13 N 3 O 3 , O 15 H 15 N 3 O	180~182 135~136 223~226 151~153 130~131	76 56 59 68 79	66.16 65.87	H H 6.92 5.13	10.29 16.46	65.98 65.75 65.79 85.81 68.64	H 5.88 5.18 5.10 5.07 5.79	N N 10.35 16.55 16.52 16.53 18.43 18.53
	14 15 16 17 18	R ₁	R2 SCH COMP COMP COMP COMP COMP COMP COMP COMP COMP	O 16 H 16 N 2 O 3 O 14 H 13 N 3 O 3 C 15 H 15 N 3 O	180~182 135~136 223~226 151~153 130~131	76 56 59 68 79 71	68.70	H H 6.92	10.29 16.46	C 65.98 65.75 65.79 85.81 68.64 68.77	H H 5.88 5.18 5.10 5.07 5.79 5.70 5.67	N N 10.35 16.55 16.52 16.53 18.43 18.53
	14 15 16 17 18 19	R ₁	R2 SCH COMM COMM COMM COMM NING NIN	O 16 H 16 N 2 O 3 O 14 H 12 N 3 O 3 C 15 H 12 N 3 O 0	180~182 135~136 223~226 151~153 130~131 150~151 231~233	76 56 59 68 79 71	68.70 65.62	H H 6.92 5.13 5.77 4.72	10.29 16.46 18.49 10.93	C 65.98 65.75 65.79 85.81 68.64 68.77 68.75	H H 5.88 5.18 5.10 5.07 5.79 5.70 4.66	N N 10.35 16.55 16.52 16.53 18.43 18.53 18.42 11.02
	1 4 1 5 1 6 1 7 1 8 1 9 2 0	R ₁	R2 R2 R5 CONNy CONN	O 16 H 16 N2 O 3 O 14 H 12 N 2 O 2 C 15 H 12 N 3 O C 15 H 12 N 3 O C 16 H 12 N 2 O 2 O 14 H 14 N 2 O 3	180~182 138~136 223~226 151~153 130~131 150~151 231~233 96~97	76 56 59 68 79 71 74 59	68.70 65.62	H H 6.92 5.13 5.77 4.72 6.24	10.29 16.46 18.49 10.93	C 65.98 65.79 65.79 65.81 68.64 68.77 68.75 65.71 74.25	H H 5.88 5.18 5.10 5.07 5.79 5.70 5.67 4.66 6.19	N N 10.35 16.55 16.52 16.53 18.43 18.53 18.42 11.02

lomp.	Subs	tituent	Molecular	m.p.	Yield		Elen	nental ai	nalysis	value	
lo.	and p	osition	formula	(°C)	(%)		Calc.	(%)	Meas	sured ((%)
	R_1	R_2				С	H	N	C	H	N
2 5	н	- CH2 CH2-	C ₁₆ H ₁₆ N ₂ O	oil	6 2		マススペ; 4 0.1 2 !	-	2 4	0.124	(*1) 6
2 6	он,	он,	O.H 12 N2 O	87~88	8 2	6 5,8 3	7.3 7	1 7.0 6	65.78	7.41	1 7.1 2
2 7	a-03H1	a-03H7	'C13 H20N2O	oi1	7 6		マススペ: 2015	•	2 2	2 0. 1 5 4	(#2) 5:0
2 8	€-03H7	4-C3H7	•	179~180	8 0	70.87	9.1 5	1272	7 0.7 9	9.1 5	1278
2 9	u-04H0	n-04He	C15H24N2O	oil	7 4		マススペ; 4 8.1 8		2 4	8.18	(#3) 75
3 0	4-04Hg	6-C4 H9		85~86	7 9	7254	9.74	11.28	7248	9.79	1 1.3 4

The compounds of this invention obtained in this way have excellent insulin biosynthesis promotion action and hypoglycemic action, and are useful at 0.1-100 mg/kg with respect to human, and the effect thereof can be sustained for 24 hours or more by the administration of 0.1-100 mg/kg once a day.

For administration, preparations formed into desired agent form by conventional means used for normal formulation method are used.

Example 1

5-week-old DDY mice (males, body weight 25-30 g) comprising 5 animals per group were fasted for 16 hours, thereafter, aqueous solution or suspension of compounds of this invention (200 mg/kg) was orally administered, and 20 minutes later, streptozotocin 200 mg/kg was intravenously administered. Blood was collected from the heart on 24 hours later, blood sugar quantity was measured by glucose oxidase method and the plasma insulin quantity was measured by two antibody method. The measurement results are shown in Table 2.

Wherein, the compound number in the Table corresponds to the compound number of Reference Example.

Caution: Translation Standard is Draft Translation

Table 2		
Administered	Blood glucose (mg/dl)	Plasma Insulin (µU/ml)
compound	mean \pm S.E.M.	mean \pm S.E.M.
Normal mouse	157±6	199±40
None (control)	386±21	43±25
1	224±19 ***	176±37 *
2	157±16 ***	153±46
3	260±33 *	213±48 *
4	248±47 *	192±54
10	263±36 *	201±38 *
12	265±32 *	253±56 *
18	166±35 ***	190±51 *
21	150±6 ***	224±30 ***
24	193±41 **	173±63
25	210±39 **	184±48 *
26	267±53	220±37 **
*: P < 0.05, **: P	< 0.01, ***: P < 0.001	

Example 2

meta-aminobenzamide (compound 2)	100 pts.
calcium hydrogenphosphate	58.5 pts.
crystalline cellulose	50 pts.
corn starch	40 pts.
calcium stearate	1.5 pts.

Above components were thoroughly mixed, and tablets, 250 mg per tablet (containing 100 mg effective component) was formed by conventional method. This is used as a hypoglycemic agent.

Example 3

A 40 % aqueous solution of meta-aminobenzylbenzamide (compound 21) was prepared, and 2 ml each thereof was sealed into ampoules and sterilised. This is used as a hypoglycemic injection.

J57-21320 (unexamined)

Caution: Translation Standard is Draft Translation

Rising Sun Communications Ltd. Terms and Conditions

Rising Sun Communications Ltd. shall not in any circumstances be liable or responsible for the accuracy or completeness of any translation unless such an undertaking has been given and authorised by Rising Sun Communications Ltd. in writing beforehand. More particularly, Rising Sun Communications Ltd. shall not in any circumstances be liable for any direct, indirect, consequential or financial loss or loss of profit resulting directly or indirectly from the use of any translation or consultation services by the customer.

7

Rising Sun Communications Ltd. retains the copyright to all of its' translation products unless expressly agreed in writing to the contrary. The original buyer is permitted to reproduce copies of a translation for their own corporate use at the site of purchase, however publication in written or electronic format for resale or other dissemination to a wider audience is strictly forbidden unless by prior written agreement.